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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,226	06/29/2001	Eric J. Benjamin	AM100155	9422

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EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,226	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *15-22,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14, 23, and 26-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's response filed on December 14, 2004 wherein no amendment is filed, i.e., no claims are amended, cancelled, or newly submitted.

Currently, claims 1-66 are pending in this application.

As indicated in the previous Office Action June 2, 2004, claims 15-22 and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species. Note that the elected specie is the specific compound recited in claim 23. Thus, claim 25 is also drawn to a non-elected species since the active pharmacological agent, raloxifene, tamoxifen, droloxifene, arzoxifene or CP 336156 is not the elected species. Therefore, claims 15-22 and 24-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-14, 23, and 26-66 are currently under examination on the merits.

Applicant's remarks filed December 14, 2004 with respect to the rejection of Claim 34 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitation, i.e., for lack of antecedent basis of record stated in the Office Action dated June 2, 2004 have been fully considered and found persuasive to remove the rejection. Therefore, the said rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 55-66 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular and specific pharmaceutical agent such as the compound of formula herein, in combination with a filler, disintegrant, wetting agent, and a lubricant or a glidant in specific amounts herein formulated into a pharmaceutical composition herein, does not reasonably provide enablement for **any** pharmaceutical agents having various and substantially different physical, chemical, and physiological properties, being used with a filler, disintegrant, wetting agent, and a lubricant or a glidant in specific amounts herein formulated into a pharmaceutical composition herein. Note that **any** pharmaceutical agents broadly encompass those known and unknown pharmaceutical compounds with any carriers and excipients as of the instant filing date, as well as those future known compounds, for reasons of record stated in the Office Action dated June 2, 2004.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required

undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors, as clearly discussed in the previous Office Action.

Response to Argument

Applicant's arguments filed December 14, 2004 with respect to this rejection under 35 U.S.C. 112, first paragraph of record in the previous Office Action have been fully considered but are not deemed persuasive as further discussed below.

Applicant argues that "[t]he present claims recite formulations comprising specific percentages of one or more components, namely, a filler, disintepant, wetting agent, lubricant and/or glidant" and "[t]hus, novel formulations are being claimed". Nonetheless, Applicant also argues that "the claimed formulations may or may not include an active agent (e.g., claims 1)". Applicant's argument is not found persuasive. Note that claim 1 herein is drawn to a pharmaceutical carrier or excipient system (composition) or a pharmaceutical formulation. Thus, the phrase "pharmaceutical" recites essential structure that is necessary to give life, meaning and vitality to a claim" (see *Kropa v. Robie*, 88 UPSQ 478, 480-481, (CCPA 1951). Therefore, a pharmaceutical is necessarily present in the pharmaceutical carrier or excipient system (composition) or pharmaceutical formulation claimed herein.

As pointed out in the rejection, the claims are seen to lack of full enablement for **any** pharmaceutical agents having various and substantially different physical, chemical, and physiological properties, being used with a filler, disintegrant, wetting agent, and a lubricant or a glidant in specific amounts herein formulated into a pharmaceutical composition herein. Note that **any** pharmaceutical agents broadly

encompass those known and unknown pharmaceutical compounds with any carriers and excipients as of the instant filing date, as well as those future known compounds.

Applicant also asserts that "although the specification discloses a number of specific active agents for use with the claimed formulations, one of ordinary skill would be able to identify other suitable active agents for use in the formulation".

Contrary to Applicant's assertion, since the instant claims are not limited to the specific examples in the specification, in the absence of fully recognizing the identity of what the active agent is, one of skill in the art would be unable to fully make and use the claimed pharmaceutical system herein. As noted in the prior Office Action, the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. *Genentech*, 108 F.3d at 1366, also states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Moreover, for those future known compounds necessarily require additional or future research to establish or verify their usefulness. Furthermore, in view of drug-drug interactions occurring with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse

consequences" (see the right column of page 51 of the book cited). Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 112, first paragraph, for lack of scope of enablement. Therefore, said rejection is adhered to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 23, 26-31, and 43-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (5,780,497, or 5,880,137, or EP 0802184 A1, or EP 0802183 A1, PTO-1449 submitted September 28, 2001) in view of Sawicka (Pharmazie 1991, vol.46 page 519-521, PTO-1449 submitted September 28, 2001).

Miller et al. (5,780,497) discloses that the active substituted indole compounds of the general structural formula therein such as the instant elected compound are useful in pharmaceutical compositions containing a pharmaceutically acceptable carrier or excipients to be administered to a mammal. See for example, '497: abstract, col.2 – col.4, and claims 5-7. Miller et al. also teaches broadly a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a lubricant, and a glidant including the instant preferred

excipients such as lactose, microcrystalline cellulose, magnesium stearate, and sulfate and Miller et al. teaches that the preparation of the formation comprising the instant compound in various oral forms with these well known excipients is **conventional** to an ordinary skilled artisan in pharmaceutical science (see especially col.7 lines 23-51).

The prior art does not expressly disclose the employment of the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein. The prior art does not expressly disclose the pharmaceutical composition herein further comprising an antioxidant.

Sawicka teaches that adding an antioxidant to a pharmaceutical composition is well known in the art and the stability of a pharmaceutical formulation may be increase by antioxidant addition. See abstract and the entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein, and to further add an antioxidant to a pharmaceutical composition herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein since it is known that a pharmaceutical composition comprising the instant compound and a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a

lubricant, and a glidant based on the prior art. Moreover, the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered conventional to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Further, one having ordinary skill in the art at the time the invention was made would have been motivated to further add an antioxidant to a pharmaceutical composition herein since adding an antioxidant to a pharmaceutical composition is well known in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument

Applicant's remarks filed February 27, 2004 with respect to this rejection of claims 1-14, 23, and 25-31 made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to claim 1-14, 23, 26-31, and 43-66, over the prior art as further discussed below.

Applicant's argument that the there is no motivation or suggestion to determine or optimize the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in the instant claimed composition has been

considered but is not found persuasive. As discussed above, the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered conventional to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. The teachings of Miller et al. regarding that making various formulations comprising the instant compound and those well-known excipients is known to be conventional, clearly support the examiner's position in the rejection.

Moreover, Applicant's Examples 1-9 of the specification at pages 27-32 herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. As discussed above, it has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Furthermore, the record contains no unexpected results showing the criticality and significance of the instant claimed ranges of well-known carriers or excipients used in the claimed composition herein. In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir.1990). See MPEP § 716.02 - § 716.02(g) for a discussion of criticality and unexpected results. It is noted that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d

135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

Applicant's remarks/arguments filed December 14, 2004 with respect to the rejection of claims 32-42 under 35 U.S.C. 103(a) as being unpatentable of record in the previous Office Action have been fully considered and found persuasive to remove the rejection as to claims 32-42 since the specific range of each ingredient in the pharmaceutical composition recited in these claims are not seen to be obvious over the cited prior art. Thus, the rejection of these particular claims is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 23, and 26-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-7 of U.S. Patent No. 5,780,497 in view of Sawicka (Pharmazie 1991, vol.46 page 519-521).

Although the conflicting claims are not identical, they are not patentably distinct from each other for the same reasons as discussed in the 103(a) set forth above.

Claims 1-14, 23, and 26-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of U.S. Patent No. 5,880,137 in view of Sawicka for the same reasons as discussed in the 103(a) set forth above.

Thus, the instant claims 1-14, 23, and 26-66 are deemed to be obvious over the 5-7 of U.S. Patent No. 5,780,497 in view of Sawicka, or claim 5 of U.S. Patent No. 5,880,137 in view of Sawicka.

In view of the rejections to the pending claims set forth above, no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
February 22, 2005